Attorney Docket No. 407T-895820US

#18
5/14/03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
Ben Shen, et al.	Examiner: Kathleen M. Kerr
Application No.: 09/477,962	Art Unit: 1652
Filed: January 5, 2000	LETTER TO OFFICIAL DRAFTSPERSON
For: BLEOMYCIN GENE CLUSTER COMPONENTS AND THEIR USES	

Attn:
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicant hereby submits 19 sheets of formal drawings to be made of record in the above-identified case.

Respectfully submitted,

Irene Pleasure, J.D., Ph.D.
Reg. No. 45,506

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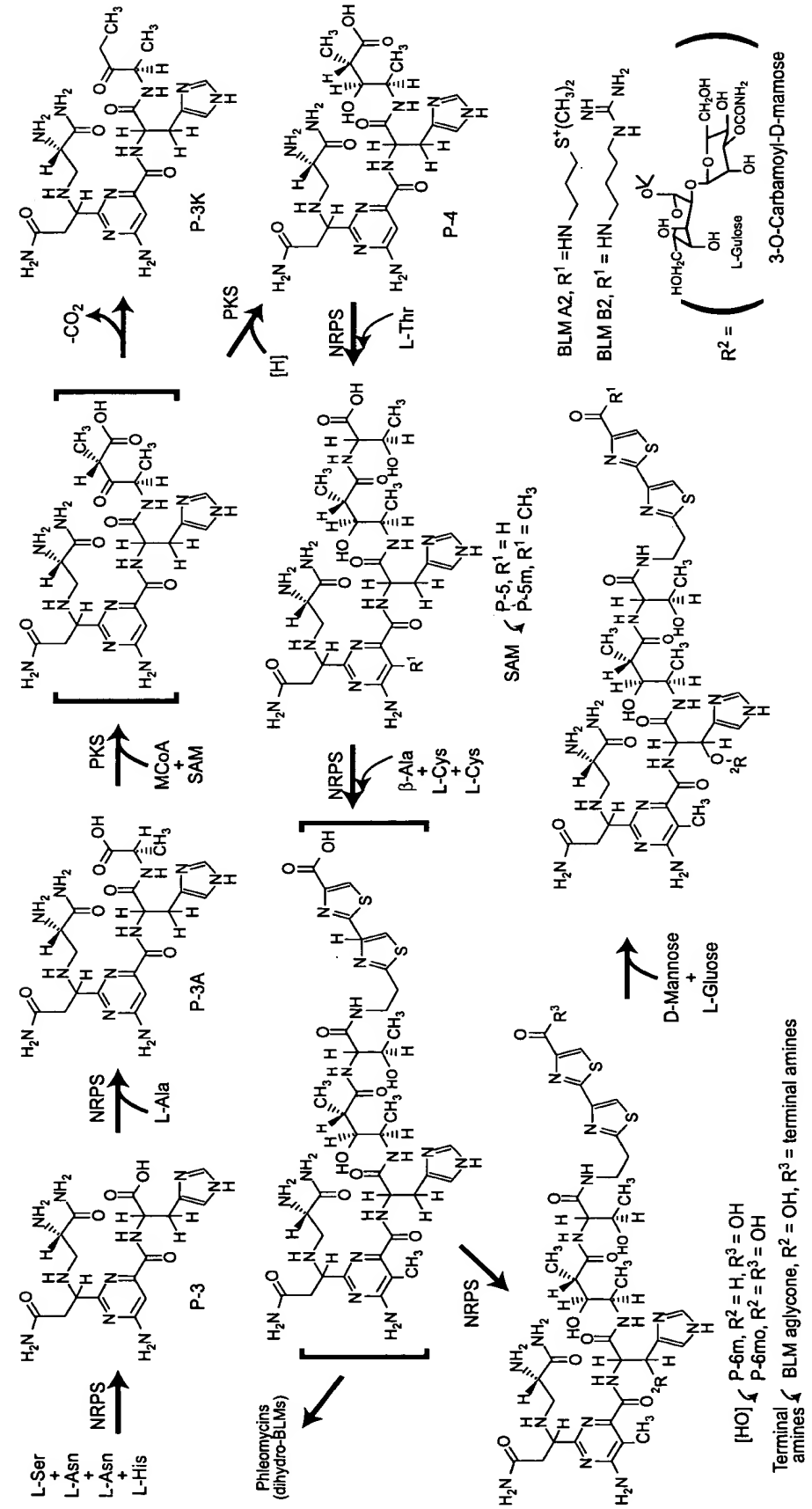


Fig. 1A

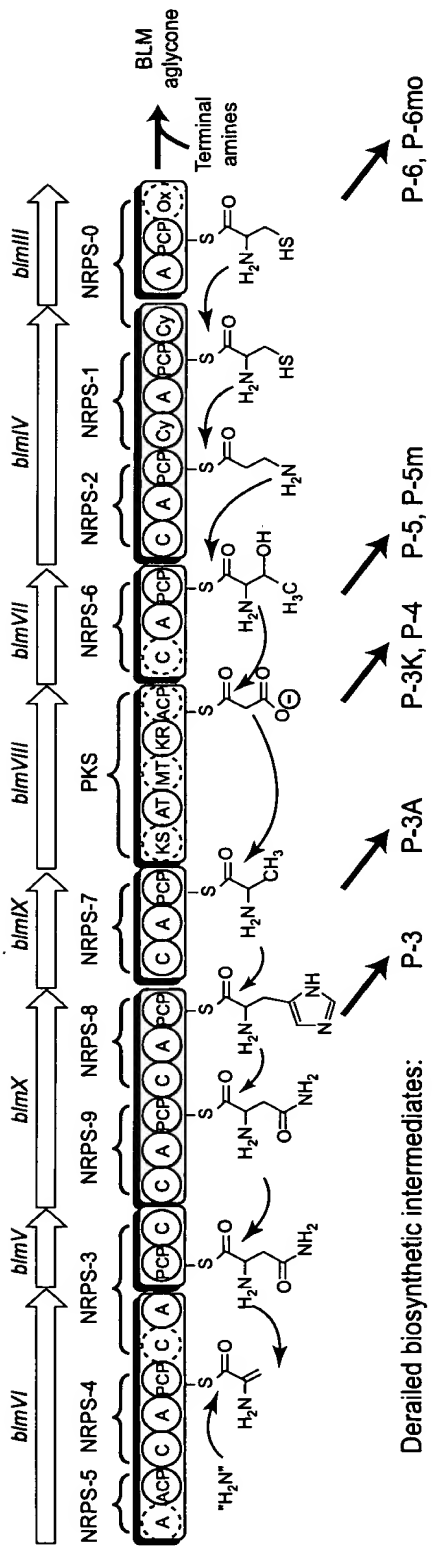

BLM aglycone
Terminal amines
P-6, P-6mo
P-5, P-5m
P-3K, P-4
P-3A
P-3
Derailed biosynthetic intermediates:
blmVI
blmV
blmX
blmIX
blmVIII
blmVII
blmIV
blmIII
NRPS-5
NRPS-4
NRPS-3
NRPS-9
NRPS-8
NRPS-7
PKS
NRPS-6
NRPS-2
NRPS-1
NRPS-0
"H2N"

Fig. 1B

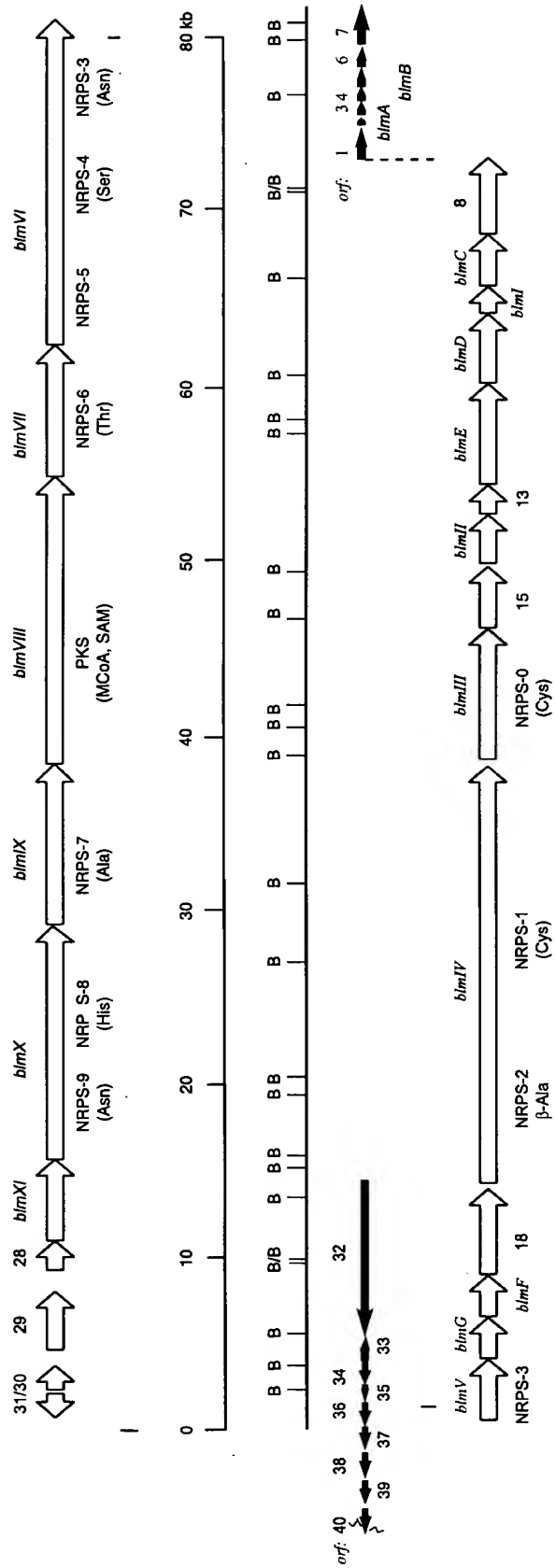


Fig. 2

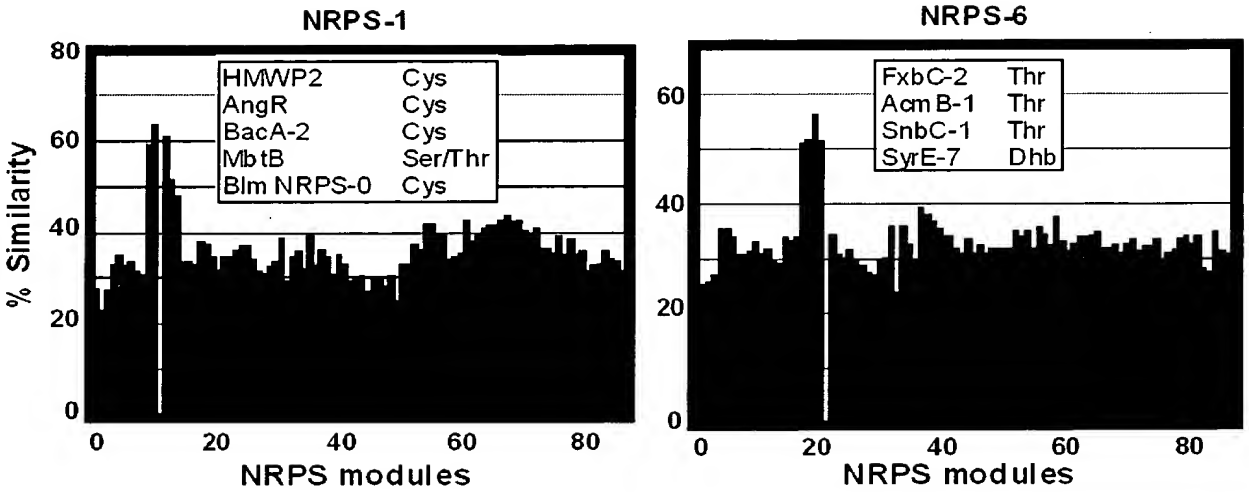


Fig. 3A

NRPS module	Substrate	Residues (PheA numbering) (16) 236	239	278	299	301	322	330	331
HMWP2	Cys	L	Y	N	M	S	M	I	W
AngR	Cys	L	Y	N	M	S	M	I	W
BacA-2	Cys	L	Y	N	L	S	L	I	W
MbtB	Ser/Thr	M	L	N	A	G	L	V	H
Blm NRPS-0	**Cys**	L	Y	H	L	G	L	P	W
Blm NRPS-1	**Cys**	L	Y	N	L	S	L	I	W
SyrE-7	Dhb	F	W	N	V	G	M	V	H
AcmB-1	Thr	F	W	N	V	G	M	V	H
SnbC-1	Thr	F	W	N	I	G	M	V	H
FxbC-2	Thr	F	W	N	V	G	M	V	H
Blm NRPS-6	**Thr**	F	W	S	V	G	M	I	H

Fig. 3B

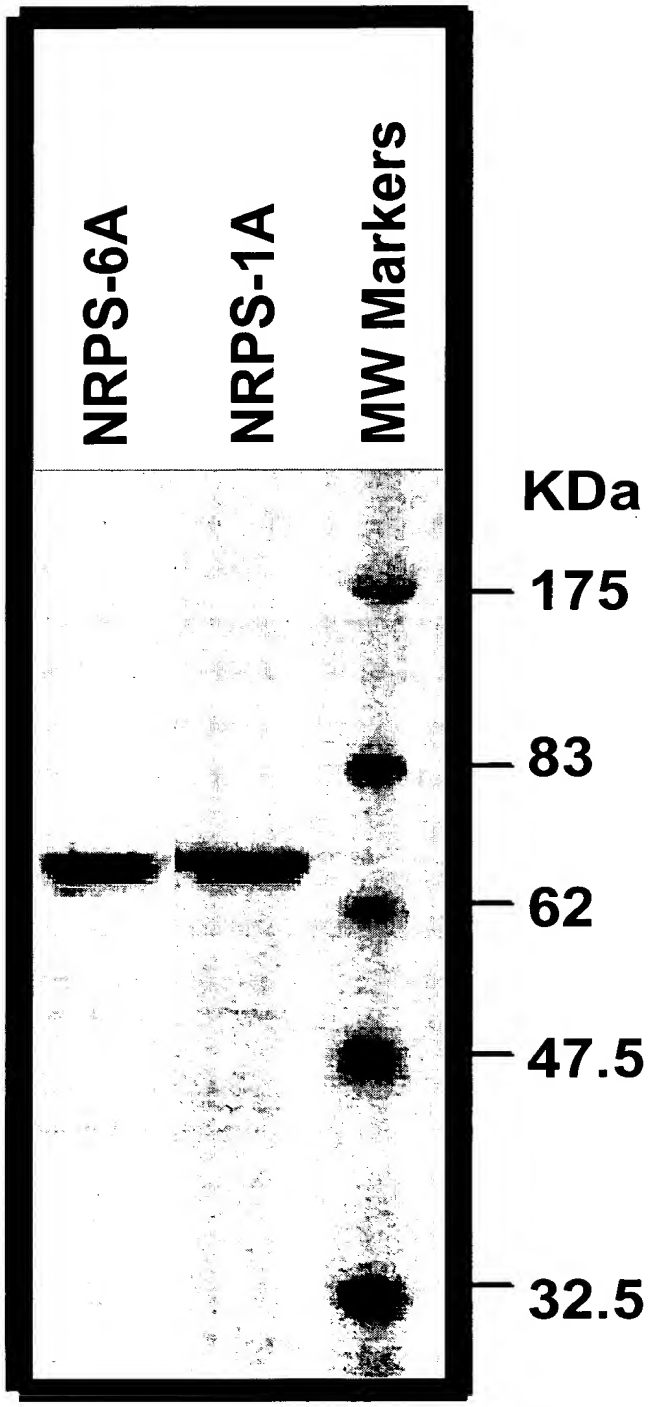


Fig. 3C

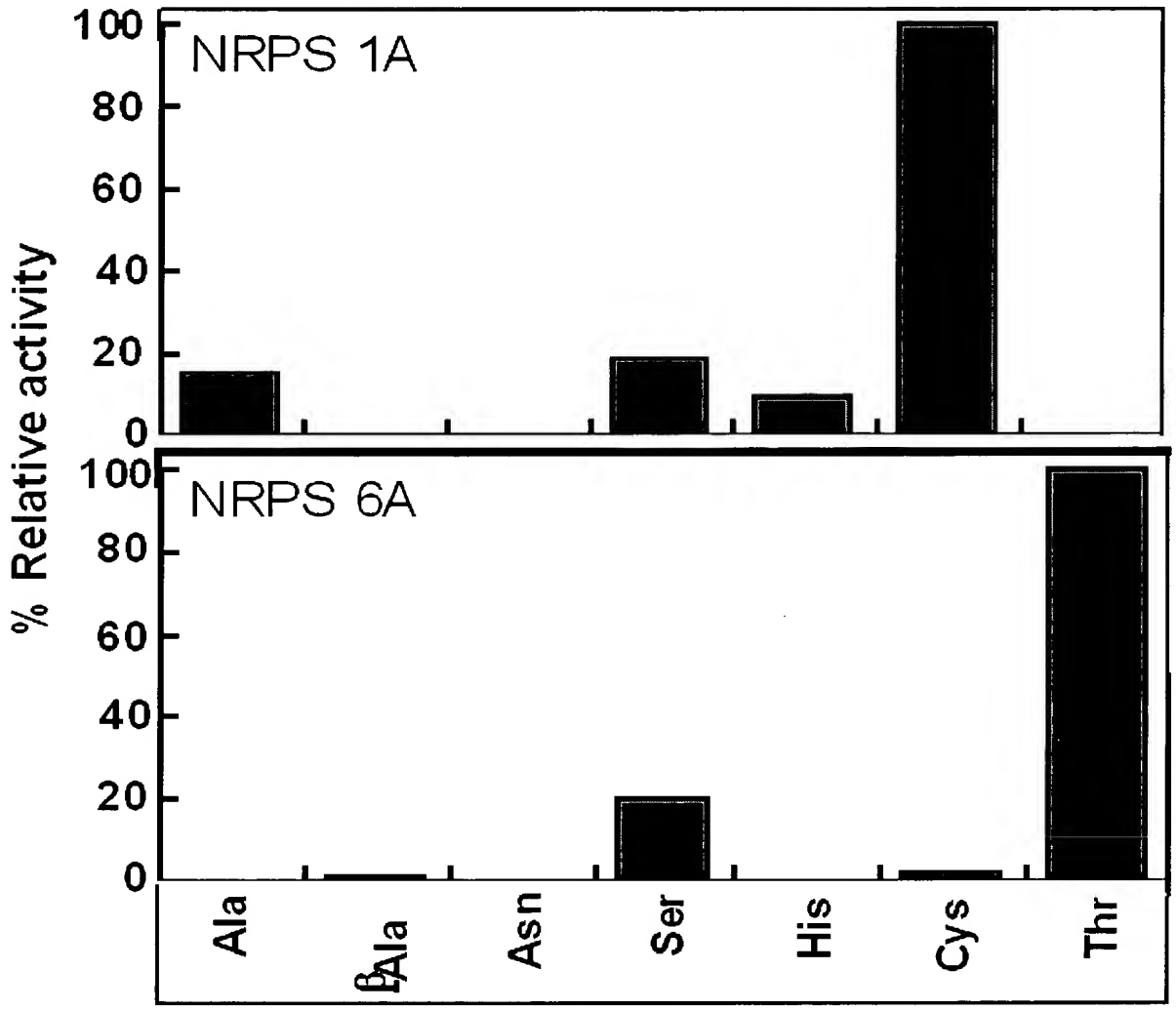


Fig. 3D

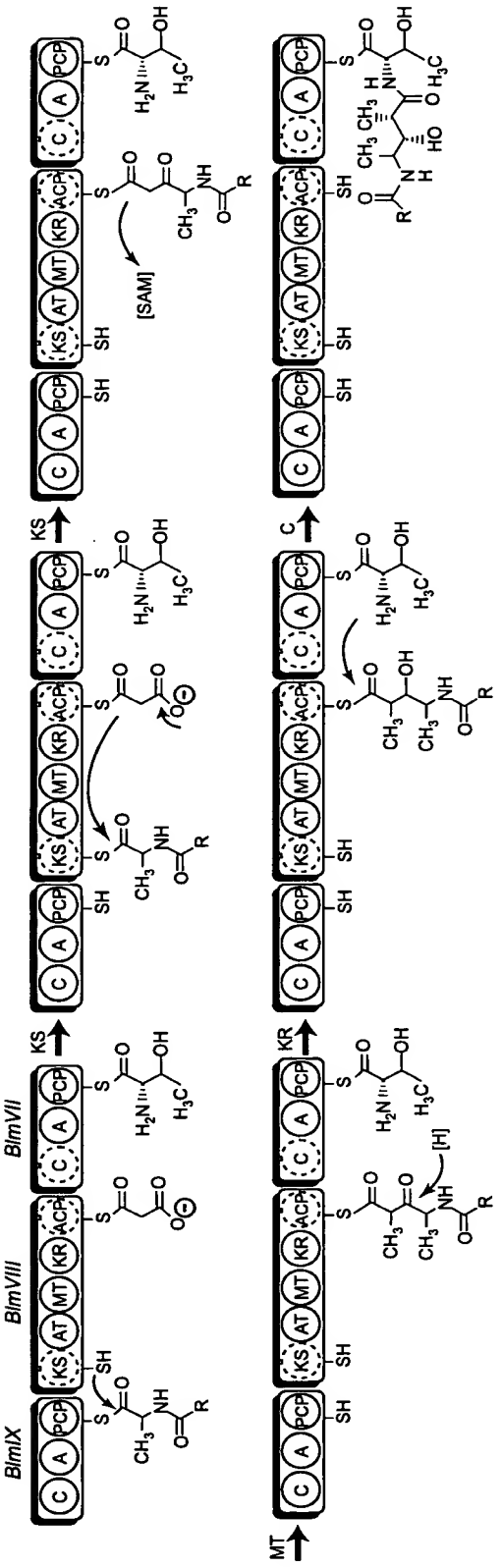


Fig. 4

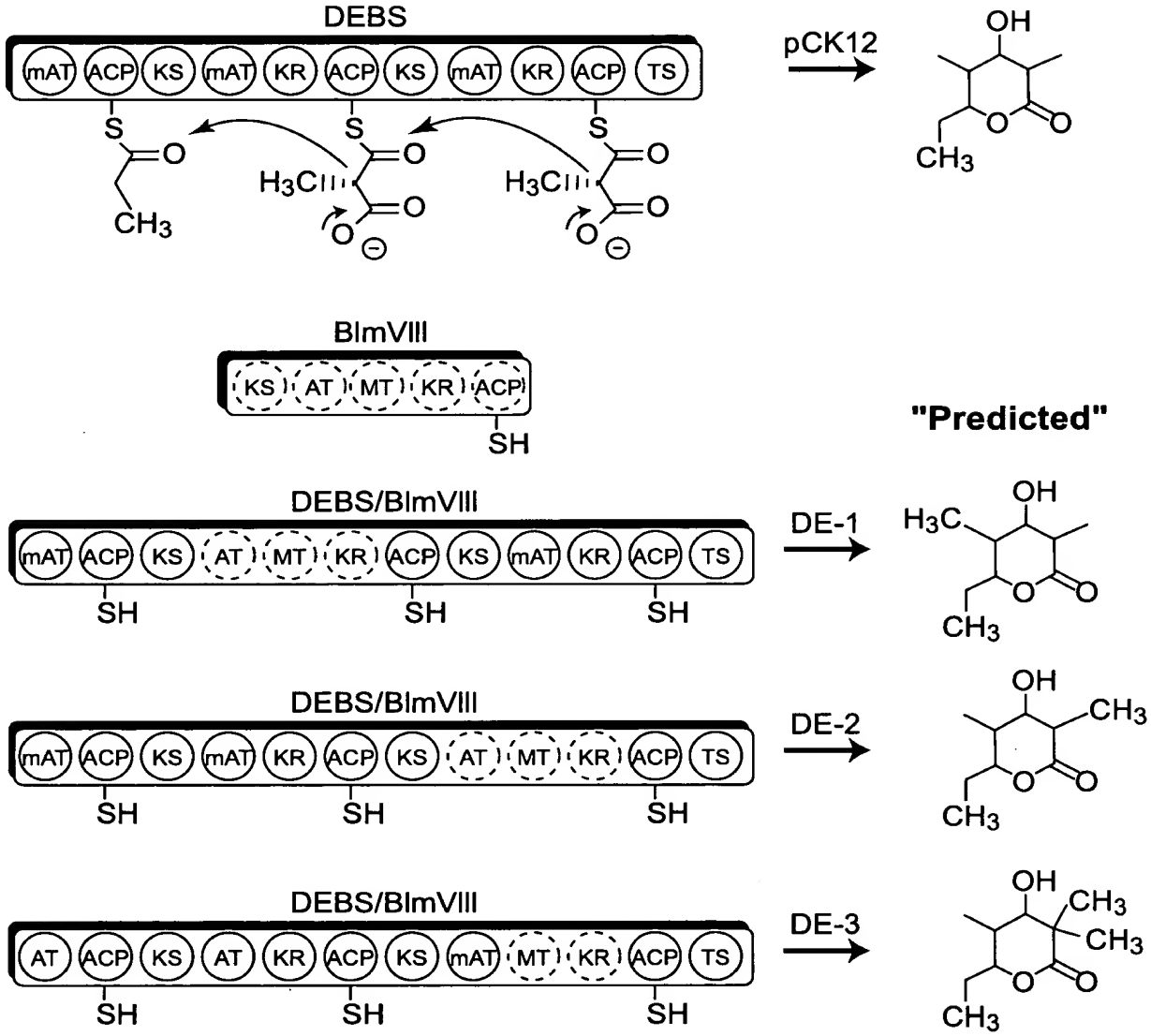


Fig. 5

Fig. 6A

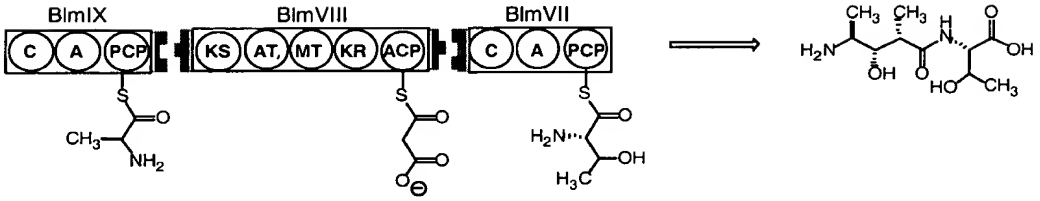


Fig. 6B

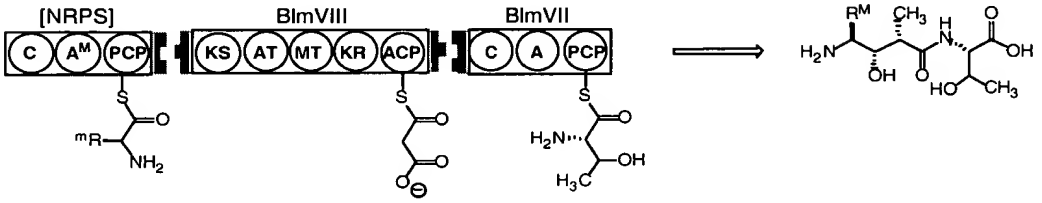


Fig. 6C

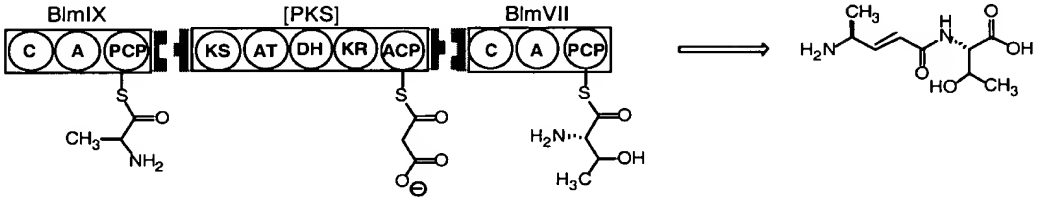


Fig. 6D

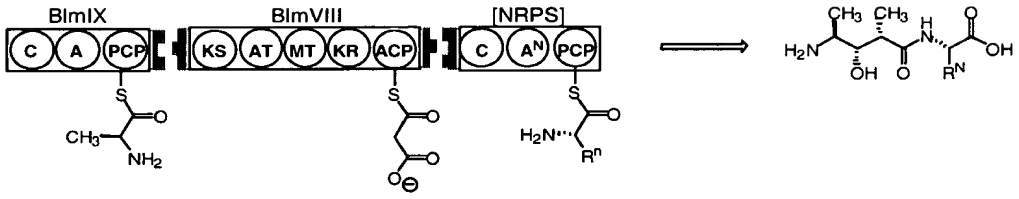


Fig. 6E

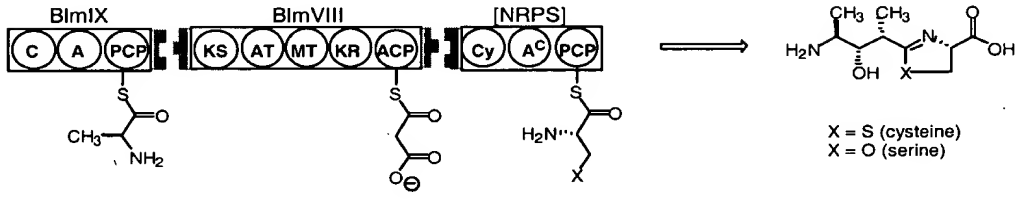
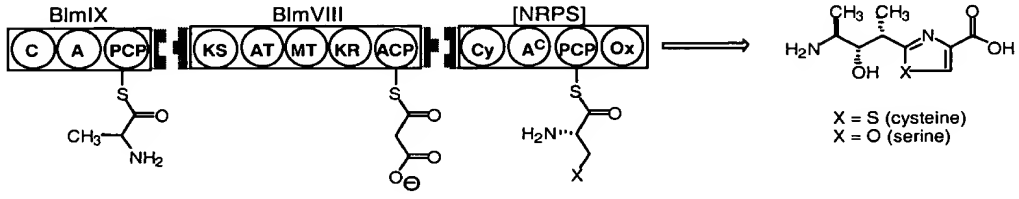


Fig. 6F



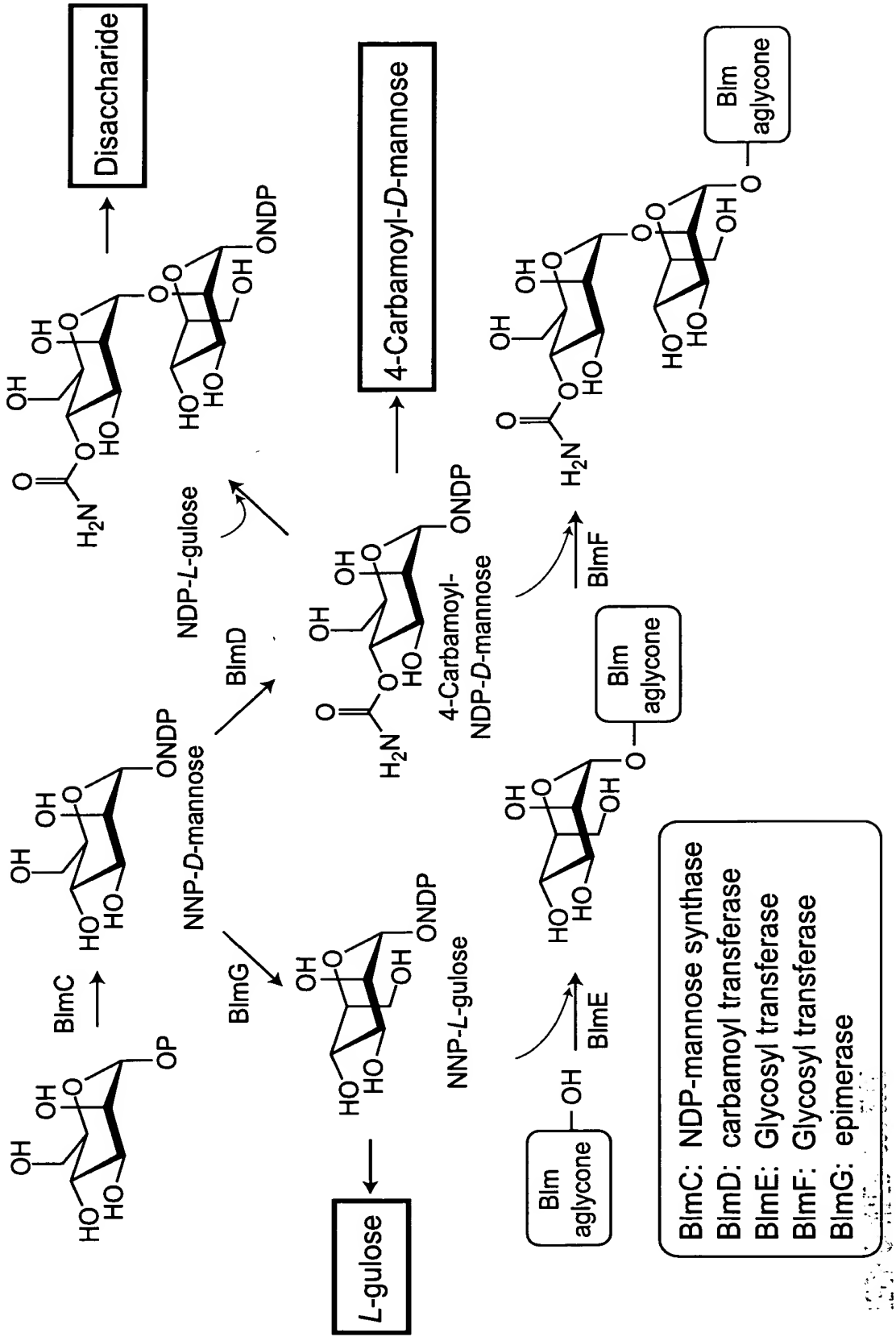


Fig. 7

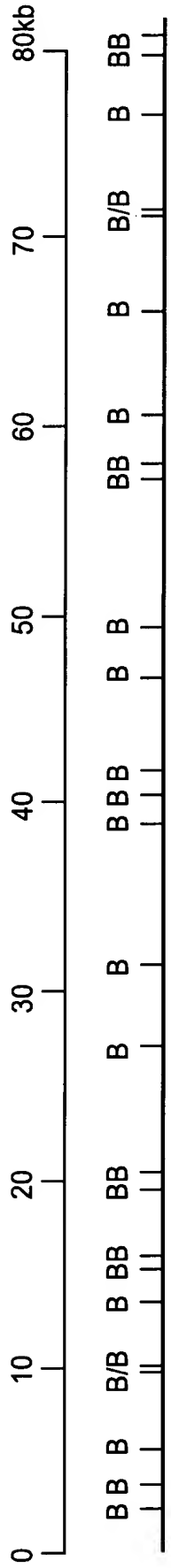


Fig. 8A

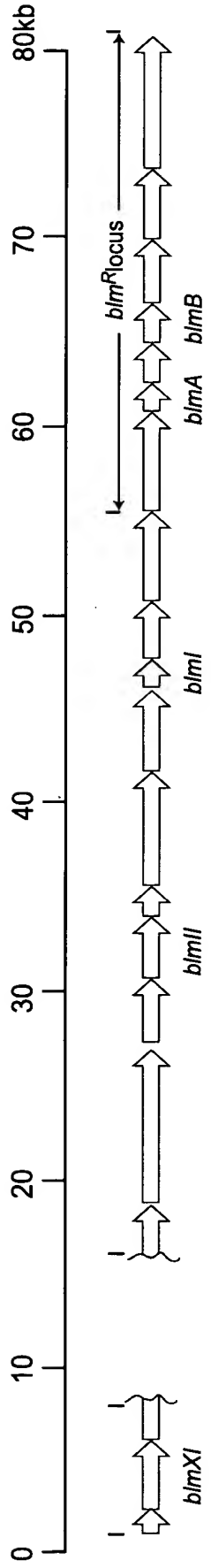


Fig. 8B

```
                                                                -18      RBS
                                                                 CC GGACGG CGGCCCGCTC
ATGAGCGCCCCCGCGGGGGCGAGCGGACCCGGCGCCGCGGCGCTCGAACGCGACATCGCCGCGATCTGGGCCGAGACCCTCGGCAGGGACAGCGTC 93
M  S  A  P  R  G  E  R  T  R  R  R  A  L  E  R  D  I  A  A  I  W  A  E  T  L  G  R  D  S  V
GGCCCGCACGAGGACTTCGCCGCGCTGGGCGGCAACTCCATCCACGCCATCAAGATCACCAACCGGGTGGAGGAACTCGTCGACGCCGAGCTG 186
G  P  H  E  D  F  A  A  L  G  G  N  S  I  H  A  I  K  I  T  N  R  V  E  E  L  V  D  A  E  L
TCCATCCGCGTCCTGCTCGAGACGCGCACCGTGGCCGGCATGACGGACCACGTCCACGCCACGCTCACGGGGGAGCGGGACCGGTGA          273
S  I  R  V  L  L  E  T  R  T  V  A  G  M  T  D  H  V  H  A  T  L  T  G  E  R  D  R  *
```

Fig. 8C

```
Grs-2      3045-ISIGTEYVAPRTMLEGKLEEIWKDVLGLQRVGIHDDFFTIGGHSL-3089
Srfa-3      960-DQLAEEWIGPRNEMEETIAQIWSEVLGRKQICIHDDFFALGGHSL-1004
Vir-S       557-GRSVEGRGVPRTPQQEILASLFAEVLGLSKVGIHEDFFDLGGHSL- 601
Saf-B      1661-LDPGQDYLAPRNELEARIAAIWEGLLRRERVGVHDSFFDLGGNSL-1705
BlmI          1-MSAPRGERTRRRALERDIAAIWAETLGRDSVGPHEDFAALGGNSI-  45
consensus     1-i  g eyvapR  le  ia iw evLgr rvGiHddFf lGGhSl-  45

Grs-2      3090-KAMAVISQVHKECQTEVPLRVLFETPTIQGLAKYIEETDTEQYMA-3134
Srfa-3     1005-KAMTAVPH.QQELGIDLPVKLLFEAPTIAGISAYLKNGGSDGLQD-1048
Vir-S       602-LATRLTSRIRTVLGAEIAVRDLFEAPTVEALAETLEEAREVRPAL- 646
Saf-B      1706-LATRLATRLAATLQVQAGVRTVFEHRTVAAQAAHFTQATKTHQAH-1750
BlmI         46-HAIKITNRVEELVDAELSIRVLLETRTVAGMTDHVHATLTGERDR-  90
consensus    46-kAmrv srv   l  ev vrvlfE pTvagla  i  g t     -  90
```

Fig. 9

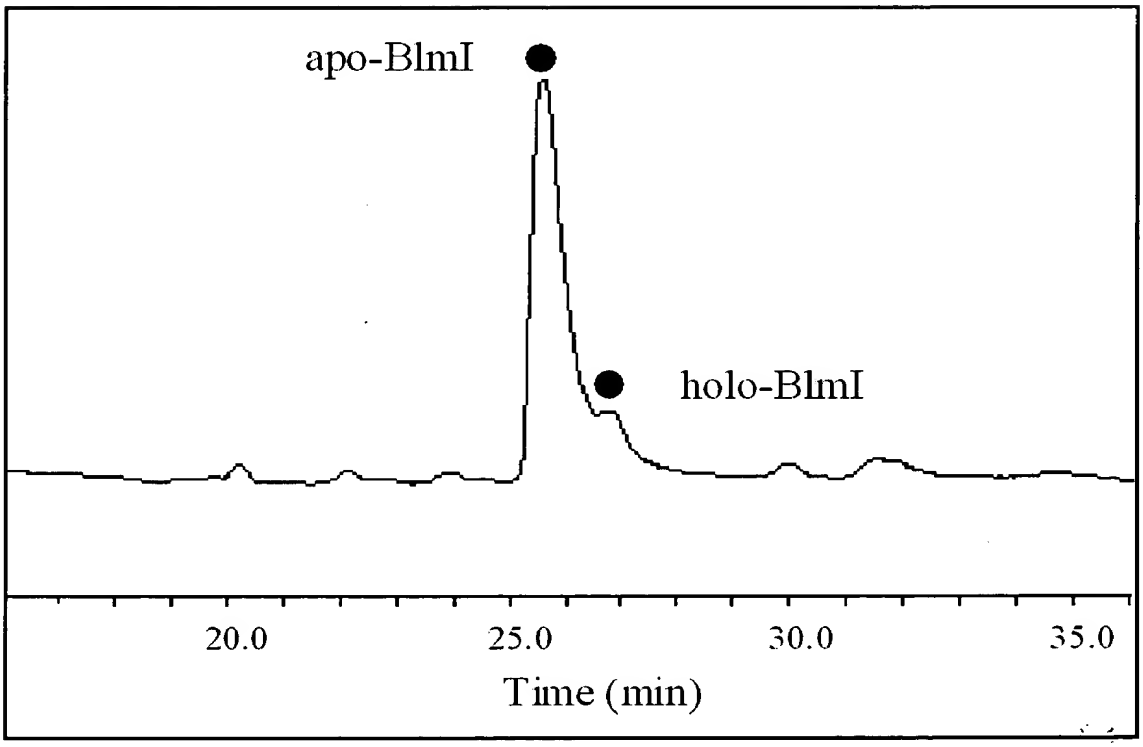


Fig. 10A

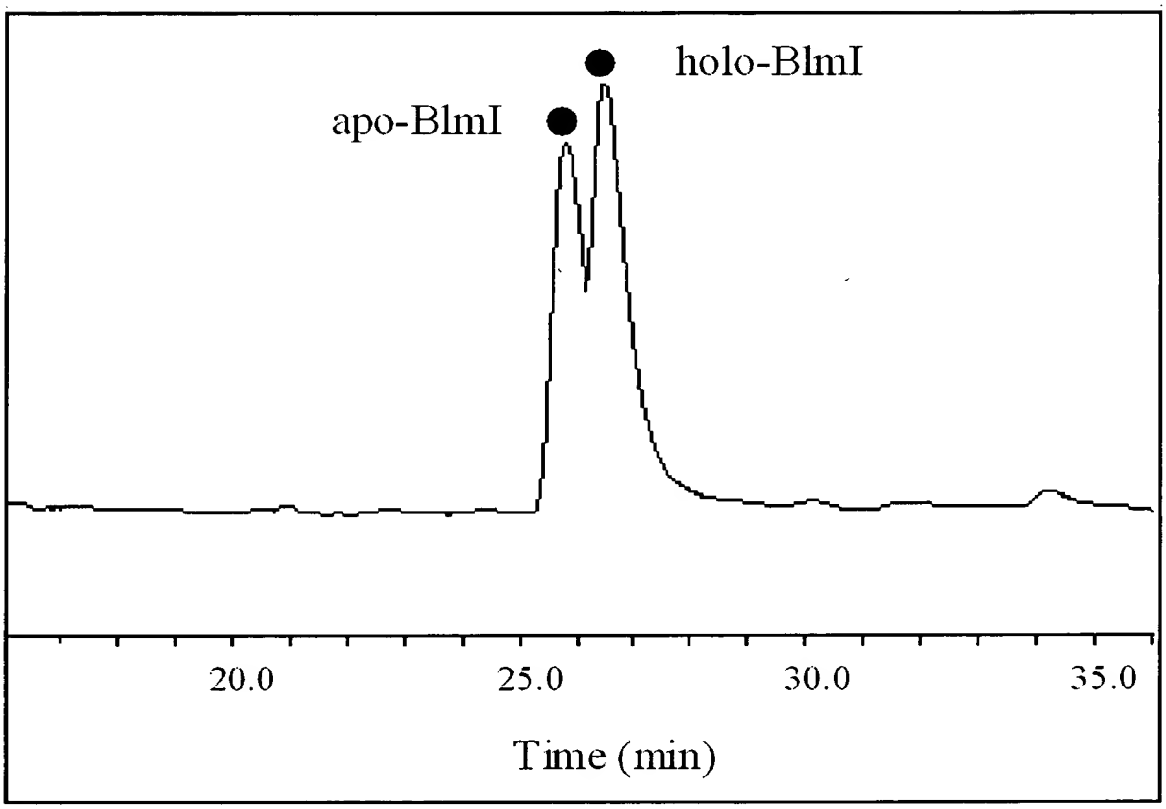


Fig. 10B

Nonreiterative Type I Modular Protein Template

Fig. 11A
PKS

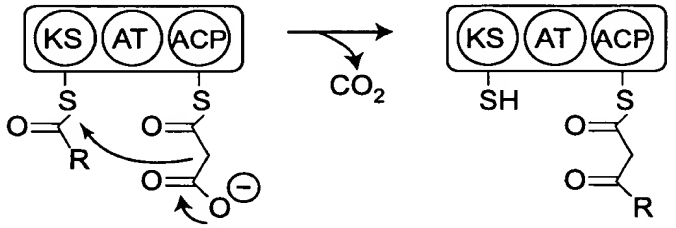
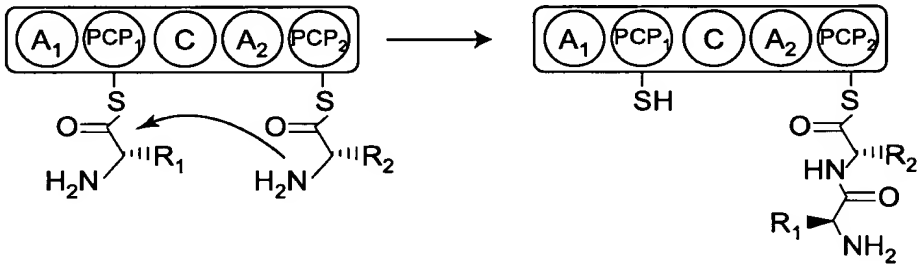


Fig. 11B
NPRS



Iterative Type II Protein Complex

Fig. 11C
PKS

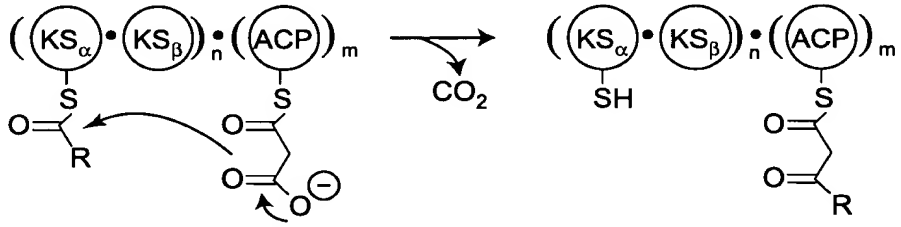
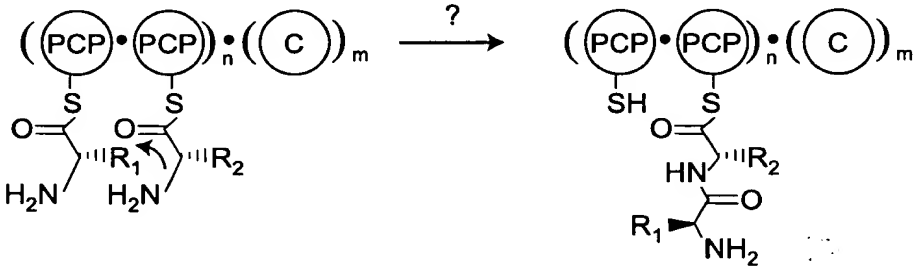


Fig. 11D
NPRS



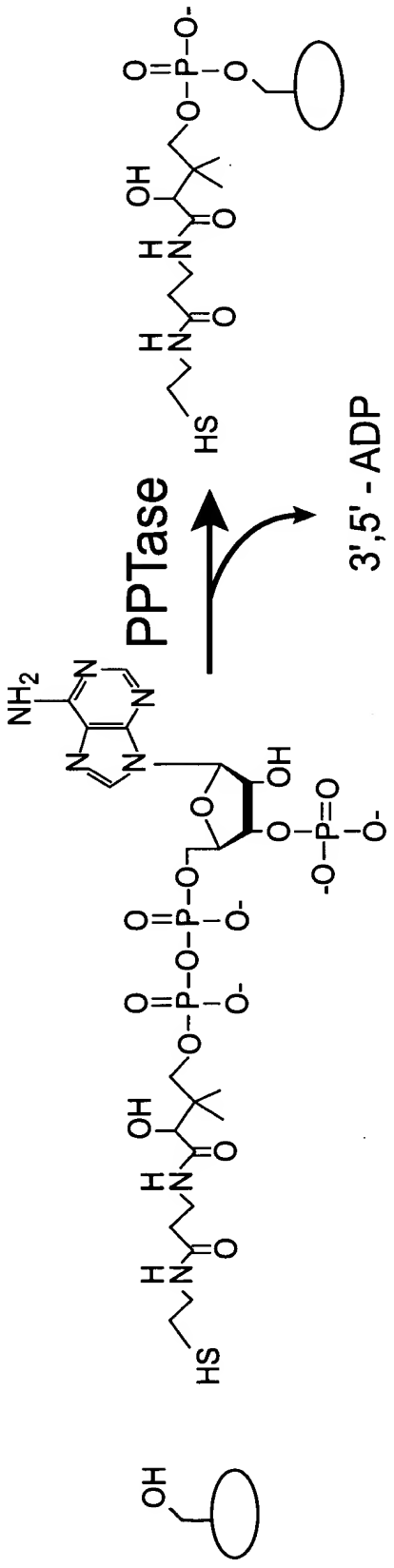


Fig. 12

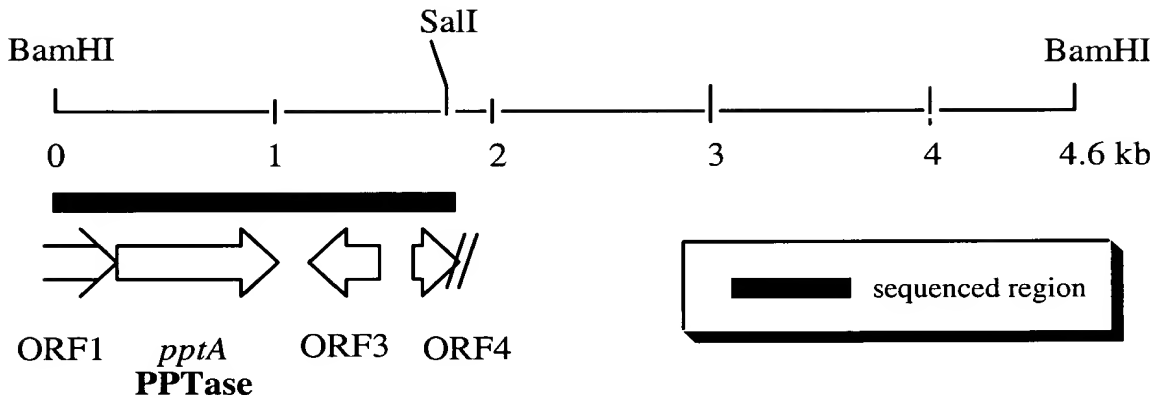


Fig. 13